Message

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Subject: tomorrow's RASS seminar
Attachments: DIB0001; Luke et al 2010.pdf

FYI, for those interested in tomorrow seminar by Reeder Sams and Hisham El-Masri, the paper that their seminar is based on is attached.
Sue

Luke et al 2010.pdf

FYI.
----- Forwarded by Kate Guyton/DC/USEPA/US on 02/02/2011 12:24 PM -----

From: "SOT Headquarters" <SOTHQ@toxicology.org>
To: Kate Guyton/DC/USEPA/US@EPA
Date: 02/02/2011 11:15 AM
Subject: RASS Telecon Wednesday February 9, 2011

Dear RASS Members

Our Spring series continues on February 9th (3:00 pm Eastern) with another Webinar! Drs. Hisham El-Masri and Reeder Sams in the Office of Research and Development of the US EPA will present "Development of a Quantitative Model Incorporating Key Events in a Hepatotoxic Mode of Action to Predict Tumor Incidence". This work represents an insightful application of biologically-based dose response (BBDR) modeling to evaluate and inform a common mode of action across several chemicals. The work was published in 2010 Toxicological Sciences 115(1), 253 - 266, so most of you should be able to access the manuscript from the SOT home page.

The logistics for logging in to the webinar are provided below along with the abstract. You are still encouraged to use conference rooms whenever feasible or possible to provide opportunity for more participants. The file for the presentation will be available for download at its usual location by Monday February 7th. The files are located in the "Downloads" section of the RASS homepage:
http://www.toxicology.org/ISOT/SS/RiskAssess/downloads.asp
In the event that link does not work directly in your browser, go to the SOT homepage (www.toxicology.org), choose "Members/Scientists" from the orange banner boxes across the top of the page. Then click on the "Access Specialty Sections" box on the right-hand side. From the drop-down menu of specialty sections that appear, choose "Risk Assessment". Once on the RASS homepage, click on "Downloads" (directly under the logo banner) between "Photo Gallery" and "Links".

I hope that you will be able to join us on February 9th for this next webinar on another important and timely topic. PLEASE NOTE that we will NOT have a Webinar next month due to the 50th anniversary annual meeting in Washington DC. The series will start again in April.

Annie

Annie M. Jarabek
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Risk Assessment Specialty Section (RASS)
Monthly *Webinar*

Wednesday February 9 from 3:00 to 4:30 p.m. (EST)
(See below for Instructions on Webinar Access)

Development of a Quantitative Model Incorporating Key Events in a Hepatotoxic Mode of Action to Predict Tumor Incidence

Hisham El-Masri
National Health and Environmental Effects Research Laboratory (NHEERL)
US EPA

Reeder Sams
National Center for Environmental Assessment (NCEA)
US EPA

Abstract

Biologically based dose-response (BBDR) modeling of environmental pollutants can be utilized to inform the mode of action (MOA) by which compounds elicit adverse health effects. Chemicals that produce tumors are typically labeled as either genotoxic or nongenotoxic. Though both the genotoxic and the nongenotoxic MOA may be operative as a function of dose, it is important to note that the label informs but does not define a MOA. One commonly proposed MOA for nongenotoxic carcinogens is characterized by the key events cytotoxicity and regenerative proliferation. The increased division rate associated with such proliferation can cause an increase in the probability of mutations, which may result in tumor formation. We included these steps in a generalized computational pharmacodynamic (PD) model incorporating cytotoxicity as a MOA for three carcinogens (chloroform, CHCl3; carbon tetrachloride,CCL4; and N,N-dimethylformamide, DMF). For each compound, the BBDR model is composed of a chemical-specific physiologically based pharmacokinetics (PBPK) model linked to a PD model of cytotoxicity and cellular proliferation. The rate of proliferation is then linked to a clonal growth model to predict tumor incidences. Comparisons of the BBDR simulations and parameterization across chemicals suggested that significant variation among the models for the three chemicals arises in a few parameters expected to be chemical specific (such as metabolism and cellular injury rate constants). Optimization of model parameters to tumor data for CCL4 and DMF resulted in similar estimates for all parameters related to cytotoxicity and tumor incidences. However, optimization of the CHCl3 data resulted in a higher estimate for one parameter (BD) related to death of initiated cells. This implies that

additional steps beyond cytotoxicity leading to induced cellular proliferation can be quantitatively different among chemicals that share cytotoxicity as a hypothesized carcinogenic MOA. (These views represent those of the authors and do not represent policy of the US EPA).

Topic: Risk Assessment Specialty Section (RASS) - Monthly Webinar
Date and Time: February 9, 2011 3:00 pm, Eastern Standard Time (New York, GMT-05:00)
Event number: Personal Matters / Ex. 6
Event password
Event address for attendees:
https://ai Personal Matters / Ex. 6

Teleconference information

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